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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/923,917	08/06/2001	Alexander Varshavsky	GPCG-P01-017	9016

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EXAMINER	
BURKHART, MICHAEL D	
ART UNIT	**PAPER NUMBER**
1633	

DATE MAILED: 09/07/2005

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/923,917	VARSHAVSKY ET AL.	
	Examiner	Art Unit	
	Michael D. Burkhart	1633	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *05 May 2005*.

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-114* is/are pending in the application.

4a) Of the above claim(s) *1-65* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *66-114* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *1/24/02* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

Response to Amendment

The amendments of 5/5/05 and 6/20/05 have been entered. Claims 1-114 are pending, claims 1-65 have been withdrawn, and claims 66-114 are currently under examination.

Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (a) the invention was known or used by others in this country, or patented or described in a printed publication in this or a foreign country, before the invention thereof by the applicant for a patent.
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

Claims 66-67, 69-71, 73, 76, 78, 81-83, 85-88, 90, 93, 95, 98-100, 102-105, 107, 110, and 112 are rejected under 35 U.S.C. 102(a) as being anticipated by Wittke et al (reference AS of the IDS dated 10/31/02). In light of MPEP 2128.02 and applicants evidence of the journal in question being received by the NLM on 8/19/1999, the prior art date of the Wittke et al reference has been changed to 8/16/1999, the date the journal was received by the USPTO library. Hence Wittke et al is now applied as before, except as a 102(a) reference. Claims 70, 85, and 102 have been included in this rejection because upon further consideration, Wittke et al teach the use of a transcription factor as reporter moiety in a split-Ub assay (see page 2528, second column, third paragraph).

Claims 66-67, 69, 71, 73, 76, 81-83, 86-88, 90, 93, 98-100, 103-105, 107, and 110 are rejected under 35 U.S.C. 102(b) as being anticipated by Johnsson et al (in The Yeast Two-Hybrid System, 1997). This rejection is maintained for reasons of record and for reasons outlined below.

Response to Arguments

Applicant's arguments filed 5/5/2005 have been fully considered but they are not persuasive. Applicants argue the Johnsson et al reference is not enabling for the claimed invention, due to the lack of a working example of library screening in the methods and vectors disclosed by Johnsson et al. Applicants point out that Johnsson et al teach that library screening and other applications "remain to be explored" (found on page 327 rather than 328, as indicated by applicants). Applicants present no reasoning as to why Johnsson et al does not meet the other factors in determining enablement (i.e. the Wands factors) and are silent as to why merely substituting the members of a library (i.e. a cDNA library) into the disclosed vectors would present a problem to those skilled in the art. Indeed, cDNA libraries were available commercially or could be routinely made at the time Johnsson et al was published (see Aronheim et al below), and could be inserted into the disclosed screening system via the construct(s) and cloning sites disclosed by Johnsson et al (i.e. *SalI-BstXI* as detailed on page 319 and illustrated in Fig. 19-2). Therefore, the only elements that need be "explored" are the source of the library and choosing suitable cloning sites. These are well-known elements in molecular biology and are clearly within reach of the skilled artisan.

New Grounds of Rejection

Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

Claims 68, 70, 84, 85, 101, and 102 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wittke et al and Johnsson et al in view of Wickens et al (U.S. patent 5,750,667, 1998) and Stagljar et al (PNAS, 1998)

The claims are as described in the previous Office Action (12/1/04) except the reporter moiety may be TRP1, CAN1, CYH2, a transcription factor, or a fluorescent marker.

The teachings of Wittke et al and Johnsson et al are as described in the previous Office Action and applied as before. Wittke et al teaches the specific use of URA3 and transcription factors as reporter moieties (see 102 (a) rejection above) and yeast stains defective in *trp1* (Table

2). Johnsson et al teaches the same, except transcription factors as reporter moieties. Wittke and Johnsson et al do not teach the specific reporters TRP1, CAN1, CYH2, or a fluorescent marker. Johnsson does not teach the use of a transcription factor.

Wickens et al teaches the use of the TRP-1 yeast selection marker in a fusion protein system to assay protein-RNA interactions (paragraph bridging column 13 and 14).

Stagljar et al teaches the use of transcription factor, PLV, as a reporter in a split-ubiquitin assay for protein-protein interactions (see abstract and second column, first full paragraph, page 5187).

The claimed methods of characterizing proteins that bind to a target protein are essentially disclosed by Wittke et al and Johnsson et al with the exception of the above reporter moieties. The ordinary skilled artisan, seeking a method workable in other cell types or yeast strains that are *trp1*-defective, would have been motivated to use other reporter moieties with the split-ubiquitin methods of Wittke et al and Johnsson et al because Stagljar et al teaches the method to be a flexible assay for protein-protein interactions without the limitations of the yeast two-hybrid assay. It would have been obvious for the skilled artisan to do this because of the known benefit of having a reporter moiety as taught by Wittke et al and Johnsson et al. Given the teachings of the cited references and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, absent evidence to the contrary, that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 72, 74, 75, 79, 80, 89, 91, 92, 96, 97, 106, 108, 109, 113, and 114 rejected under 35 U.S.C. 103(a) as being unpatentable over Wittke et al and Johnsson et al in view of Pack et al (U.S. patent 6,294,353, 2001, and corresponding PCT, WO96/13583, published 1996), Rossi et al (PNAS, 1997), and Aronheim et al (Mol. Cell. Biol., 1997).

The claims are as described in the previous Office Action (12/1/04) except the host cell may be mammalian, plant, or insect, and the number of library members may be 500 or greater.

The teachings of Wittke et al and Johnsson et al are as described in the previous Office Action and applied as before. Wittke et al and Johnsson et al do not teach the use of mammalian, plant, or insect host cells, or the use of libraries with 500 or more members.

Pack et al teach the use of mammalian, plant, and insect cells as host cells for vectors expressing protein domains that may associate and form active complexes (see claims 20-21 and page 7 of WO 96/13583 along with claims 19-21 of 6,294,353).

Rossi et al teach an assay for protein-protein interactions in human cells based on the complementation of defective β-galactosidase peptides and the use of the method for screening libraries. See the abstract, Figures 1 and 2, and page 8410, first column, second full paragraph.

Aronheim et al disclose a method for detecting protein-protein interactions based on a SOS-recruitment system, into which the inserted a rat cDNA library of $2x10^6$ clones (members). See the abstract and page 3095, first column, second paragraph.

The claimed methods of characterizing proteins that bind to a target protein are essentially disclosed by Wittke et al and Johnsson et al with the exception of the above cell types and library size. The ordinary skilled artisan, seeking a method workable in other cell types or comprising cDNA libraries, would have been motivated to use other cell types with the split-

ubiquitin methods of Wittke et al and Johnsson et al because Rossi et al teaches the advantage of using any host cell type with "its own particular milieu of competing resident proteins" (page 8410, first column). It would have been obvious for the skilled artisan to do this because of the known benefit of studying the interactions of proteins and multiprotein complexes, as detailed in Wittke et al and Johnsson et al. Given the teachings of the cited references and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, absent evidence to the contrary, that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Claims 77, 94, and 111 are rejected under 35 U.S.C. 103(a) as being unpatentable over Wittke et al, Johnsson et al, Pack et al, and Rossi et al as applied to claims 72, 74, 75, 79, 80, 89, 91, 92, 96, 97, 106, 108, 109, 113, and 114 above, and further in view of Inze et al (U.S. Patent 6,710,227, 2004, effective filing date 3/16/2000).

The claims are as described in the previous Office Action (12/1/04) except the host cell may be an *A. thaliana* or *N. tabacum* cell.

The teachings of Wittke et al, Johnsson et al are described in the previous Office Action and applied as before. The teachings of Pack et al, and Rossi et al are described above and applied as before. Wittke et al, Johnsson et al, Pack et al, and Rossi et al do not teach the use of an *A. thaliana* or *N. tabacum* cell.

Inze et al teach the use of *A. thaliana* as host cells for the preparation of a cDNA library for use in a two-hybrid screen to identify proteins which bind to CDC2aAt. See column 5, lines 20-40 and the paragraph bridging columns 28-29.

The claimed methods of characterizing proteins that bind to a target protein are essentially disclosed by Wittke et al, Johnsson et al, Pack et al, and Rossi et al with the exception of the *A. thaliana* or *N. tabacum* cell types. The ordinary skilled artisan, seeking a method workable in screening plant cDNA libraries, would have been motivated to use *A. thaliana* cells in the split-ubiquitin methods of Wittke et al and Johnsson et al because Rossi et al teaches the advantage of using any host cell type with "its own particular milieu of competing resident proteins" (page 8410, first column) and Inze et al teaches *A. thaliana* to be a suitable model system for plants and a source for cDNA library construction. It would have been obvious for the skilled artisan to do this because of the known benefit of studying the interactions of proteins and multiprotein complexes, as detailed in Wittke et al and Johnsson et al, and the suitability of *A. thaliana* cells for this purpose, as taught by Inze et al.. Given the teachings of the cited references and the level of skill of the ordinary skilled artisan at the time of applicants' invention, it must be considered, absent evidence to the contrary, that the ordinary skilled artisan would have had a reasonable expectation of success in practicing the claimed invention.

Conclusion

No claims are allowed.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Michael D. Burkhart whose telephone number is (571) 272-2915. The examiner can normally be reached on M-F 8AM-5PM.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Dave Nguyen can be reached on (571) 272-0731. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

Michael D. Burkhart
Examiner
Art Unit 1633

CELIAN QIAN
PATENT EXAMINER